

#2/99

61-42

IN THE SPECIFICATION

At page 1, lines 5-6, please delete [continuation-in-part application of copending] and replace with divisional application of copending United States application Serial No. 09/194,285, filed April 12, 1999, ^{US patent 6,355,479} which is based on.

IN THE CLAIMS

✓ / ✓ / ✓ /
Please cancel claims 1-60 and 85-113.

✓ / ✓ /
Please add new claims 114-148.

--114. A method for activating CD4⁺ T cells in vitro, the method comprising:

a) contacting a synthetic antigen presenting cell (APC) with a peptide library in vitro for a sufficient time to generate a peptide-loaded MHC class II heterodimer for activating CD4⁺ T cells, wherein the APC comprises:

i) a MHC class II α -chain gene operably linked to a first promoter in a vector capable of expressing a MHC class II α -chain;

ii) a MHC class II β -chain gene operably linked to a second promoter in a vector capable of expressing a MHC class II β -chain, wherein upon expression of the α -chain and β -chain genes, the α -chain and β -chain form a MHC class II heterodimer capable of loading a peptide; and

iii) at least one accessory molecule gene operably linked to a third promoter in a vector capable of

expressing an accessory molecule, wherein at least one of the Class II genes and accessory molecule gene is lacking from the APC, wherein the expressed MHC class II heterodimer and accessory molecule are present on the surface of the APC in an amount sufficient for activating CD4⁺ T cells when a peptide is loaded on the MHC Class II heterodimer; and

Q2
cont. b) contacting the peptide-loaded MHC class II heterodimer of step a) with CD4⁺ T cells, thereby inducing the contacted CD4⁺ T cells to proliferate and differentiate into activated CD4⁺ T cells.

115. The method of claim 114 further comprising:

c) separating the activated CD4⁺ T cells from the APC.

116. The method of claim 115 further comprising the step of adding the activated CD4⁺ T cells to an acceptable carrier or excipient to form a suspension.

117. The method of claim 116 further comprising the step of administering the suspension to a patient.

118. The method of claim 114 wherein the synthetic APC is produced by the method according to claim 61.

119. The method of claim 114 wherein the synthetic APC lacks a gene coding for at least one of the α -chain, the β -chain and the accessory molecule genes.

120. The method of claim 114 wherein the α - and β - chain genes are of human origin.

121. The method of claim 114 wherein the synthetic APC is an insect cell.

122. The method of claim 121 wherein the insect cell is selected from the group consisting of Spodoptera and Drosophila.

124. The method of claim 123 wherein the costimulatory molecule is B7.1 or B7.2.

125. The method of claim 114 wherein the accessory molecule gene encodes an adhesion molecule.

126. The method of claim 125 wherein the adhesion molecule is ICAM-1, ICAM-2, ICAM-3 or LFA-3.

127. The method of claim 114 wherein the accessory molecule gene encodes a survival molecule.

128. The method of claim 127 wherein the survival molecule is Fas ligand or CD70.

129. The method of claim 128 further comprising a second accessory molecule gene for a second accessory molecule.

130. The method of claim 129 wherein the first accessory molecule is a costimulatory molecule and the second accessory molecule is an adhesion molecule.

131. The method of claim 129 wherein the first accessory molecule is a costimulatory molecule and the second accessory molecule is an survival molecule.

132. The method of claim 129 wherein the first accessory molecule is a survival molecule and the second accessory molecule is an adhesion molecule.

133. The method of claim 129 further comprising a third accessory molecule gene for a third accessory molecule.

134. The method of claim 133 wherein the first accessory molecule is a costimulatory molecule, the second accessory molecule is an adhesion molecule, and the third accessory molecule is a survival molecule.

135. A method for activating CD4⁺ T cells in vitro, the method comprising:

1. The first step is to identify the problem. This involves understanding the current situation and what needs to be changed.

a) contacting a cell fragment derived from the APC of a synthetic antigen presenting cell (APC) with a peptide library in vitro for a sufficient time to generate a peptide-loaded MHC class II heterodimer for activating CD4⁺ T cells, wherein the APC comprises:

i) a MHC class II α -chain gene operably linked to a first promoter in a vector capable of expressing a MHC class II α -chain;

ii) a MHC class II β -chain gene operably linked to a second promoter in a vector capable of expressing a MHC class II β -chain, wherein upon expression of the α -chain and β -chain genes, the α -chain and β -chain form a MHC class II heterodimer capable of loading a peptide; and

iii) at least one accessory molecule gene operably linked to a third promoter in a vector capable of expressing an accessory molecule, wherein at least one of the Class II genes and accessory molecule gene is lacking from the APC, wherein the expressed MHC class II heterodimer and at least one accessory molecule are operably associated on the fragment for activating CD4⁺ T cells in an amount sufficient for activating CD4⁺ T cells when a peptide is loaded on the MHC Class II heterodimer; and

b) contacting the peptide-loaded MHC class II heterodimer of step a) with CD4⁺ T cells, thereby inducing the contacted CD4⁺ T cells to proliferate and differentiate into activated CD4⁺ T cells.

136. The method of claim 135 further comprising:

c) separating the activated CD4⁺ T cells from the APC.

137. The method of claim 136 further comprising the step of adding the activated CD4⁺ T cells to an acceptable carrier or excipient to form a suspension.

138.. The method of claim 137 further comprising the step of administering the suspension to a patient.

139. The method of claim 135 wherein the cell fragment is derived from a synthetic APC produced by the method according to claim 61.

140. A method of altering a CD4⁺ T cell-mediated immune response to treat a condition in a patient comprising:

- analyzing the patient for patient-specific cytokine profile;
- collecting CD4⁺ T cells from the patient;
- contacting the CD4⁺ T cells with a synthetic

antigen presenting cell (APC) for a sufficient time to activate CD4⁺ T cells, wherein the APC comprises:

- i) a MHC class II α -chain gene operably linked to a first promoter in a vector capable of expressing a MHC class II α -chain;

- ii) a MHC class II β -chain gene operably linked to a second promoter in a vector capable of expressing a MHC class II β -chain, wherein upon expression of the α -chain and β -chain genes, the α -chain and β -chain form a MHC class II heterodimer capable of loading a peptide; and

- iii) at least one accessory molecule gene operably linked to a third promoter in a vector capable of expressing an accessory molecule, wherein at least one of the Class II genes and accessory molecule gene is lacking from the APC, wherein the expressed MHC class II heterodimer and accessory molecule are present on

1. The first group of people who are affected by this disease are those who have a family history of the disease.

NS
Cont

the surface of the APC in a sufficient amount to activate CD4⁺ T cells when a peptide is loaded onto the heterodimer in vitro thereby inducing the contacted CD4⁺ T cells to proliferate and differentiate into activated CD4⁺ T cells that produce a functionally opposing cytokine profile to the profile obtained in step a); and

d) returning the activated CD4⁺ T-cells to the patient.

141. The method of claim 140 wherein the condition is an autoimmune disease.

142. The method of claim 141 wherein the autoimmune disease is selected from the group consisting of diabetes, multiple sclerosis, autoimmune thyroiditis, systemic lupus erythematosus, mysasthenia gravis, Crohn's disease and inflammatory bowel disease.

143. The method of claim 141 wherein the patient-specific cytokine profile is produced by a CD4⁺ Th1 type response.

144. The method of claim 143 wherein the patient-specific cytokine profile comprises the cytokine selected from the group consisting of interleukin-2, interferon- γ and tumor necrosis factor.

145. The method of claim 140 wherein the condition is an allergy.

146. The method of claim 145 wherein the allergy is selected from the group consisting of asthma and contact sensitivity.

147. The method of claim 145 wherein the patient-specific cytokine profile is produced by a CD4⁺ Th2 type response.

ag
cont.

0915094400